

CLAIMS

1. A graftable animal cell or tissue of a donor species for use in medicine, wherein said cell or tissue expresses, or is capable of being caused to express, increased amounts of endogenous complement regulatory molecules for preventing activation of complement in a recipient species.

2. A cell or tissue according to Claim 1, for use in transplantation therapy.

3. A cell or tissue as claimed in Claim 1 ~~or Claim 2~~, wherein the tissue is an organ.

4. A cell or tissue as claimed in Claim 3, wherein the organ is a heart, lung, liver, kidney, pancreas, or thyroid.

5. A cell or tissue as claimed in Claim 1 ~~or Claim 2~~, wherein the tissue is skin.

6. A cell or tissue as claimed in Claim 1 ~~or Claim 2~~ comprising isolated cells selected from islet cells, neurones, and stem cells.

7. A cell or tissue as claimed in ^{Claim 1} ~~any of the preceding Claims~~, wherein said complement regulatory molecules comprise complement regulatory proteins (CRPs).

8. A cell or tissue according to Claim 7, wherein said CRPs comprise or have the activity of one or more, of CD59, Membrane Cofactor protein (MCP), Decay Accelerating Factor (DAF; CD55), homologous restriction factor (HRF), CR1 (CD35).

9. A cell or tissue according to ~~any of Claims 1 to~~
~~8~~, wherein said donor species is a pig.

10. A cell or tissue according to ~~any of Claims 1 to~~
~~8~~, wherein said donor species is a sheep.

11. A cell or tissue according to ~~any of the preceding~~
~~claims~~, wherein the recipient species is human.

12. The use of an animal cell or tissue derived from
a donor species, and one or more complement regulatory
molecules endogenous to the donor species which can be
hyper-expressed to prevent activation of complement in a
recipient species, in the preparation of tissue graftable
into the recipient species without hyperacute rejection.

13. A method of preparing an animal cell or tissue
derived from a donor species for transplanting into a
recipient species, and/or for reducing the likelihood of
hyperacute rejection once transplanted, which comprises
causing said cell or tissue to express increased amounts of
the endogenous complement regulatory molecules sufficient to
prevent complete activation of complement in the recipient
species.

14. A method according to Claim 13, which comprises
transfecting the cell or tissue with a viral vector encoding
a complement regulatory molecule.

15. A method according to Claim 13, wherein said
complement regulatory molecule is a CRP, and which comprises
the use of cytokines or other factors acting directly or
indirectly on regulatory elements in the CRP gene to
increase expression of said CRP before, during or after

transplant.

16. A non-human transgenic animal having cells or tissue which hyper-expresses endogenous complement regulatory molecules.

5 17. A DNA molecule selected from:

(a) a pig CD59 gene or its complementary strand,

(b) a sequence substantially homologous to, or capable of hybridising to, a substantial portion of a gene defined in (a) above,

10 (c) a molecule coding for a polypeptide having the sequence of Figure 2 (SEQ ID No. 2),

(d) genomic DNA corresponding to a molecule in (a) above; and

15 (e) a fragment of a molecule defined in any of (a), (b), (c), or (d) above, other than the fragment described SEQ ID No. 1.

18. A DNA molecule selected from:

(a) a pig DAF gene or its complementary strand;

20 (b) a sequence substantially homologous to, or capable of hybridising to, a substantial portion of a gene defined in (a) above;

(c) a molecule coding for a polypeptide having the sequence of Figure 15 (SEQ ID Nos. 17-19),

25 (d) a genomic DNA corresponding to a molecule in (a) above; or,

(e) a fragment of a molecule defined in any of (a), (b), (c), or (d) above.

19. An RNA molecule comprising an RNA sequence corresponding to a DNA sequence according to Claim 17 ~~or Claim 18.~~

20. A nucleic acid probe having a sequence according to ~~any one of Claims 17 or 19,~~ and optionally including a label.

21. An isolated, purified, or recombinant polypeptide comprising a pig CD59 protein or a mutant, variant or portion thereof or encoded by a sequence according to Claims ~~17 or 19~~ or a variant thereof having substantially the same activity as the pig CD59 protein.

22. A polypeptide according to Claim 21, wherein the pig CD59 protein has the amino acid sequence defined in Figure 2. (SEQ ID No. 2).

23. An isolated, purified or recombinant polypeptide comprising a pig DAF protein or a mutant, variant or portion thereof or encoded by a sequence according to Claim ~~18 or 19~~ or a variant thereof having substantially the same activity as the pig DAF protein.

24. A polypeptide according to Claim 23 wherein the pig DAF protein has the amino acid sequence defined in Figure 15 (SEQ ID Nos 17-19)

25. An anti-pig CD59 monoclonal antibody or a labelled anti-pig CD59 monoclonal antibody.

26. A vector comprising the nucleic acid sequence of ~~any one of Claims 17 and 19.~~

27. A host cell transfected or transformed with a vector according to Claim 26.

28. The use of a vector according to Claim 27 ~~or a nucleic acid sequence according to either Claim 17 or Claim 18~~, in gene therapy and/or in the preparation of a cell or tissue for xenotransplantation.

29. A non-human transgenic animal wherein the transgene comprises the DNA of Claim 17 ~~or Claim 18~~.

30. Nucleic acid primers selected from the following, as herein defined:

	A-Pig	:	C-Pig	(SEQ ID No.3 : SEQ ID No.4)
10	Q ₀	:	Q ₁	(SEQ ID No.6 : SEQ ID No.7)
			Q _T	(SEQ ID No. 5)
	D-Pig	:	E-Pig	(SEQ ID No.8 : SEQ ID No.9)
	RT-Pig			(SEQ ID No.10)
	F-Pig	:	G-Pig	(SEQ ID No.11 : SEQ ID No.12)
15	pigxP-1	:	PigxP-2	(SEQ ID No.13 : SEQ ID No.14)

31. A method of increasing the resistance of an animal cell or tissue of a donor species to complement attack when transplanted into a recipient species, which comprises one or more of:-

(a) exposing said cell or tissue to sub-lytic complement

attack; or

(b) exposing the cell or tissue to nutrient deprivation; or

(c) applying conditions of limited anoxia to the cell or tissue; or

5 (d) exposing said cell or tissue to ionophores; or

(e) exposing said cell or tissue to exogenous chemicals,
thereby to increase the resistance of said cell or tissue to complement attack.

32. A method according to Claim ³¹~~32~~, wherein the exogenous
10 chemical is a lectin.

33. A method according to Claim 32, wherein the exogenous chemical is a cytokine or a chemokine.

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